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(54) FLUORINE-CONTAINING POLYMER AND MEDICAL-USE OXYGEN-PERMEABLE SUBSTANCE

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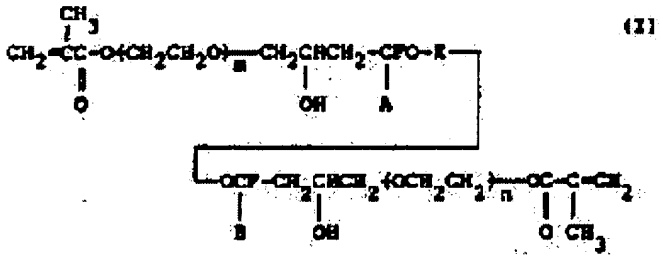
[Amendments have been incorporated into text of translation]

Specification

1. Title of the Invention: Fluorine-containing polymer and medical-use oxygen-permeable substance

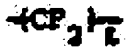
2. CLAIMS

1. A fluorine-containing polymer having oxygen permeability with a number-average molecular weight of 1000 ~ 80000, a prepared with the monomer (I) represented by general formula (I)

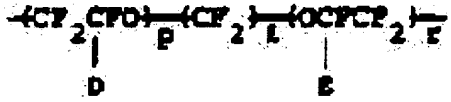


(I)

(wherein A and B are fluorine atoms or perfluoroalkyl groups, m and n are 0 or 1, and X is a group represented by the general formula



(wherein ℓ is an integer of 1 ~ 8), or the group represented by the general formula:



(wherein D and E are fluorine atoms or lower perfluoroalkyl groups, p and r are integers of 1 ~ 7, and ℓ is identical as above)).

2. A fluorine-containing polymer of Claim (1), characterized in that at least one monomer is chosen from hydrophilic monomers, silicon-containing monomer, methacrylic-group-containing monomer, and a monomer having two or more polymerizable functional groups, which is allowed to undergo copolymerization by adding to monomer (I).

3. A fluorine-containing polymer of Claim (2), wherein 5 ~ 60 wt% of monomer (I), 5 ~ 10 wt% of hydrophilic monomers, 20 ~ 55 wt% of a silicon containing monomer, 0 ~ 35 wt% of methyl or ethyl methacrylic acid and 1 ~ 10 wt% of a monomer (II) having two or more polymerizable functional groups are allowed to undergo copolymerization.

4. A fluorine-containing polymer of Claim (2) or (3), wherein the hydrophilic monomer is chosen from at least one substance of the group consisting of 2–hydroxyethyl methacrylate, polyethylene glycol monomethacrylate, glyceryl methacrylate, N-vinylpyrrolidone, methacrylic acid, and dimethylacrylamide.

5. A fluorine-containing polymer of Claim (2) or (3), wherein the silicon-containing monomer (II) is chosen from at least one substance of the group containing 3–(methacryloxy) propyltrimethoxy silane, 3–(methacryloxy) propyl-bis (trimethylsiloxy) methylsilane and 3–(methacryloxy) propyldimethoxy methylsilane.

6. A fluorine-containing polymer of Claim (2) or (3), wherein the methacrylic-group-containing monomer is an alkyl methacrylate or aralkyl methacrylate.

7. A fluorine-containing polymer of Claim (2) or (3), wherein the monomer (II) having two or more polymerizable functional groups is chosen from at least one type from the group consisting of ethylene glycol dimethacrylate, diethylene glycol dimethacrylate, triethylene glycol dimethacrylate, tetraethylene glycol dimethacrylate, allyl methacrylate, diallyl phthalate, trimethylolpropane trimethacrylate, and pentaerythritol tetramethacrylate.

8. A fluorine-containing polymer of Claims (1) ~ (7), wherein polymerization is carried out by using a radical polymerization initiator at 0.01 ~ 1.5 wt% in relation to 100 wt% of polymerization monomer.

9. A fluorine-containing polymer of Claims (1) ~ (9), wherein the oxygen permeability coefficient is 3×10^{11} to 80×10^{-11} cc.cm/cm^3.sec.mm Hg*, the index of refraction of the plate-shaped molded material is 1.35 ~ 1.52, and the Vickers hardness No. is 4 ~ 25.

10. A medical-use oxygen-permeable substance made of a fluorine-containing polymer having oxygen permeability, with a number-average molecular weight of 1000 ~ 80000, prepared with monomer (I) of Claim (1).

11. A medical-use oxygen-permeable substance made of a fluorine-containing polymer of Claim (10), wherein at least one monomer (I) is chosen from hydrophilic monomers, silicon-containing monomer, methacrylic-group-containing monomer, and a monomer having two or more

* [The unit "cm^3" is not clearly legible]

polymerizable functional groups, which undergoes copolymerization.

12. A medical-use oxygen-permeable substance made of a fluorine-containing polymer of Claim (11), wherein 5 ~ 60 wt% of monomer (I), 5 ~ 10 wt% of hydrophilic monomers, 20 ~ 55 wt% of a silicon-containing monomer, 0 ~ 35 wt% of methyl or ethyl methacrylic acid, and 1 ~ 10 wt% of a monomer having two or more polymerizable functional groups are allowed to undergo copolymerization.

13. A medical-use oxygen-permeable substance consisting of a fluorine-containing polymer of Claim (11) or (12), wherein the silicon-containing monomer is 3–(methacryloxy) propyltrimethoxy silane, 3–(methacryloxy) propyl-bis (trimethylsiloxy) methylsilane, and 3–(methacryloxy) propyldimethoxymethylsilane.

14. A medical-use oxygen-permeable substance made of a fluorine-containing polymer of Claim (10) or (11), wherein the hydrophilic monomer is chosen from at least one type from the group consisting of 2–hydroxyethyl methacrylate, polyethylene glycol monomethacrylate, glyceryl methacrylate, N-vinylpyrrolidone, methacrylic acid, and dimethylacrylamide.

15. A medical-use oxygen-permeable substance made of a fluorine-containing polymer of Claim (10) or (11), wherein the methacrylic-group-containing monomer is an alkyl methacrylate or aralkyl methacrylate.

16. A medical-use oxygen-permeable substance made of a fluorine-containing polymer of Claim (10) or (11), wherein the monomer having two or more polymerizable functional groups is chosen from at least one type from the group consisting of ethylene glycol dimethacrylate, diethylene glycol dimethacrylate, triethylene glycol dimethacrylate, tetraethylene glycol dimethacrylate, allyl methacrylate, diallyl phthalate, trimethylolpropane trimethacrylate, and pentaerythritol tetramethacrylate.

17. A medical-use oxygen-permeable substance made of a fluorine-containing polymer of Claims (10) ~ (16), wherein polymerization is carried out using a radical polymerization initiator at an amount of 0.01 ~ 1.5 wt% in relation to 100 wt% of the polymerization monomer.

18. A medical-use oxygen-permeable substance made of a fluorine-containing polymer of Claims (10) ~ (17), wherein the oxygen permeability coefficient is 3×10^{11} to 80×10^{-11} cc.cm/cm^3.sec.mm Hg, the index of refraction of the plate-shaped molded material is 1.35 ~

1.52, and the Vickers hardness No. is 4 ~ 25.

3. Detailed Description of the Invention

[Industrial Application Field]

The present invention pertains to a fluorine-containing polymer having oxygen permeability as well as to an oxygen-permeable substance for medical use made of the polymer.

An oxygen-permeable substance for medical use enabling the taking in of oxygen, and which does not rely on biological fluid (for example, blood), which is in an instable state due to the oxygen load that is physically established when oxygen is continuously supplied to a particular biological tissue, has been used. The present invention pertains to this type of fluorine-containing polymer and the oxygen-permeable substance for medical purposes.

In further detail, the present invention pertains to a medical-use oxygen-permeable substance made of fluorine-containing polymer having oxygen permeability and useful as a raw material for producing oxygen-permeable substances used for ophthalmic materials such as a hard contact lens (HCL).

[Prior Art]

Conventionally, polymethyl methacrylate (PMMA) has been widely used as HCL material due to its excellent optical properties, chemical properties, physical strength, and mechanical processability.

Since the cornea is avascular tissue, the necessary oxygen for respiratory metabolism is obtained by diffusion of the ocular blood vessel of the palpebral conjunctiva and tears when the eyes are closed. When the eyes are open, the oxygen is taken in from the air. Therefore, putting on a HCL (contact lens) forms an oxygen barrier, which might cause hyperemia, edema, and other corneal disorders. The necessary oxygen amount for the cornea is 3.5 ~ 4.8 μu (STP) / cm^3.hr.

For the conventional PMMA series HCL, since the oxygen permeability is very low, only a small HCL can be put onto the eye, which leads to the eyes having the sensation of a foreign body in them. Therefore, it is desirable to develop an oxygen-permeable substance such as HCL with a greater oxygen permeability. In recent years, a siloxane bond has been introduced into the ester portion of a methacrylic acid ester, and a silicon methacrylate series HCL with improved oxygen permeability (Kokoku No. 52-33502) has been disclosed. An oxygen-permeable HCL using butyl acetate cellulose (CAB) as the main component and an oxygen-permeable HCL using a methacrylate containing fluorine have also been disclosed (Kokai No. 57[1982]-51705).

The silicon methacrylate series HCL disclosed in Kokoku No. 52[1977]-33502 has over tens to hundreds [times greater] oxygen permeability compared with the commonly used conventional PMMA series HCL. However, the drawback is that it is easily stained by substances such as the lipids adhered thereon due to a poor hardness and hydrophilic property.

Therefore, generally, the form of copolymerization with methylmethacrylate (MMA) is adapted. If the level of silicon methacrylate increases, the oxygen permeability improves, but, the aforementioned drawbacks will become more serious. Also, the hydrophilic property is lacking on the surface due to the poor wetness property. In many cases, a hydrophilic process must be re-conducted.

On the other hand a, polymer containing fluorine has corrosion and stain resistance and has a great oxygen and carbonic anhydride permeability. By utilizing these properties, has been discovered that a HCL with high oxygen permeability can be produced from the copolymer of a monomer containing fluorine. Furthermore, an oxygen-permeable substance for medical use and the polymer for producing this oxygen-permeable substance that has superior oxygen permeability, anti-ultraviolet, open extraction surface hardness, hydrophilic property, and stain resistance, and that is comfortable to wear, has been produced.

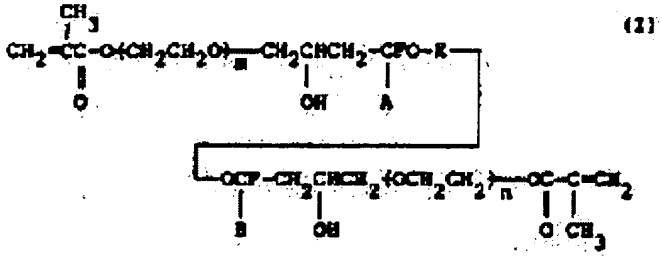
[Problems to be Solved by the Invention]

The purpose of the present invention is to provide an oxygen-permeable substance for medical use, such as HCL with superior oxygen permeability, anti-ultraviolet, penetration surface hardness, hydrophilic property, and stain resistance, and that is comfortable to wear.

Another purpose of the present invention is to provide a fluorine-containing polymer that is useful for producing said oxygen-permeable substance.

[Means for Solving the Problems]

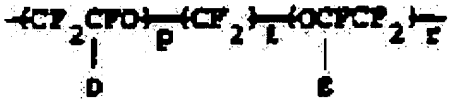
(1) A fluorine-containing polymer having oxygen permeability with a number-average molecular weight of 1000 ~ 80000 is prepared with the monomer (I) represented by general formula (I)



(I)

(wherein A and B are a fluorine atoms or perfluoroalkyl groups, m and n are 0 or 1, and X is a group represented by the general formula 

(wherein ℓ is an integer of 1 ~ 8), or the group represented by the general formula:

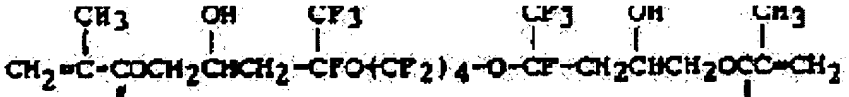


(wherein D and E are fluorine atoms or lower perfluoroalkyl groups, p and r are integers of 1 ~ 7, and ℓ is identical as above)).

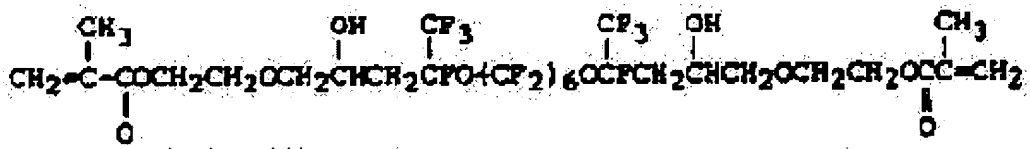
(2) The present invention relates to an oxygen-permeable substance for medical use that is made of fluorine-containing polymer.

In the present invention, examples of the lower alkyl group in the lower perfluoroalkylation [perfluoroalkyl] group include the ones having 1 to 4 carbon atoms, such as methyl, ethyl, n-propyl, and n-butyl. While p and r indicate integers of 1 to 7, respectively, it is preferred that the sum of p and r is between 2 to 10.

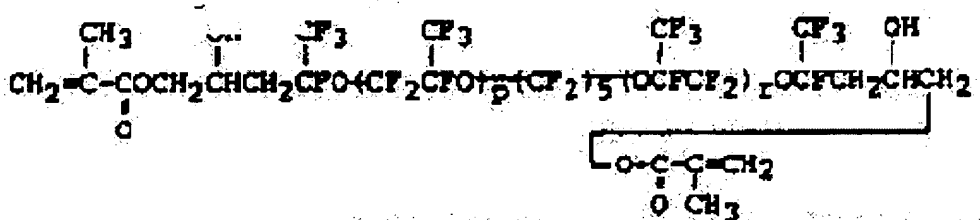
As monomer (I), which is the primary component of the polymer of the present invention, for instance, an example is given in the following:



molecular weight = 718 monomer (1)



molecular weight = 906 monomer (2)



molecular weight = 2096 (where p + r = 8) monomer (3)

The polymer of the present invention can be a polymer of said monomer (I) solely. It is also acceptable that at least one monomer is chosen from the hydrophilic monomers, silicon-containing monomer, methacrylic-group-containing monomer, and a monomer having two or more polymerizable functional groups, with monomer (I) being allowed to undergo copolymerization.

The hydrophilic monomer used for the copolymerization, can be 2–hydroxyethyl methacrylate, polyethylene glycol monomethacrylate, glyceryl methacrylate, N-vinylpyrrolidone,

methacrylic acid, and dimethylacrylamide. By introducing the hydrophilic monomer, the hydrophilic property of the resultant polymer can be improved, and interaction with body fluid components can be controlled. That is, destruction of red blood cells can be controlled.

The silicon-containing monomer can be 3–(methacryloxy) propyltrimethoxysilane, 3–(methacryloxy) propylbis (trimethylsiloxy) methylsilane, and 3–(methacryloxy) propyl dimethoxymethylsilane.

The methacrylic-group-containing monomer, can be a lower alkyl methacrylate such as methyl methacrylate and ethyl methacrylate, or an aralkyl methacrylate such as benzyl methacrylate.

The methacrylic acid derivative monomer having two or more polymerizable functional groups, can be ethylene glycol dimethacrylate, diethylene glycol dimethacrylate, triethylene glycol dimethacrylate, tetraethylene glycol dimethacrylate, allyl methacrylate, diallyl phthalate, trimethylolpropane trimethacrylate, and pentaerythritol tetramethacrylate.

The polymer of the present invention is produced by polymerizing said monomer (I) individually, a monomer can be copolymerized with other monomers as described above.

As examples of the combination of each monomer used for copolymerization, 5 ~ 60 wt% of monomer (I), 5 ~ 10 wt% of hydrophilic monomers, 20 ~ 55 wt% of a silicon-containing monomer, 0 ~ 35 wt% of methyl or ethyl methacrylic acid, and 1 ~ 10 wt% of a monomer having two or more polymerizable functional groups are preferred.

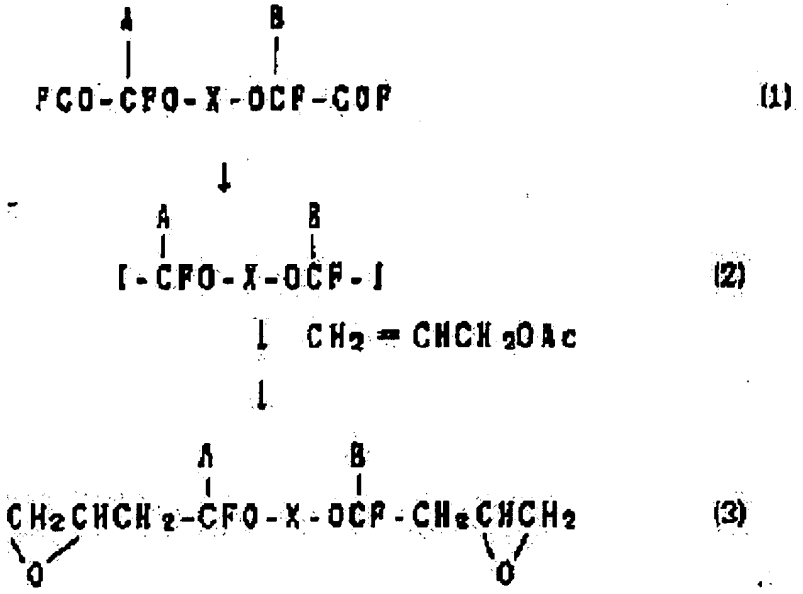
The polymerization initiator used for copolymerization can be a radical polymerization initiator such as benzoyl peroxide, t - butyl peroxide, azobisisobutyronitrile, or azobisdimethylvaleronitrile.

The polymerization is carried out by using a radical polymerization initiator at a rate of 0.01 ~ 1.5 wt% in relation to 100 wt% of the polymerization monomer. Also, each of the monomer mixtures is immersed in a dry ice – acetone bath and allowed to freez, after repeating the process of deaeration for several minutes at approximately 1 mm Hg, then allowed to melt under vacuum, and to freeze and deaerate againt The polymerization treatment is repeated several times under vacuum at a temperature of 50 ~ 110^{0}C for 12 ~ 98 hours. Repeating the polymerization process at a reduced pressure is more desirable. Concretely, the polymerization is carried out at 50^{0}C for 6 ~ 48 hours first, then at 70^{0}C for 8 ~ 24 hours, furthermore, at 90^{0}C for 5 ~ 12 hours, and finally heated at 110^{0}C and under reduced pressure (approximately 1 mm Hg) for 3 ~ 12 hours.

The polymer obtained this way has a high degree of crosslinkage, and is highly oxygen permeable. The polymer properties include a molecular weight of 1000 ~ 80000, oxygen permeability coefficient of 3 ~ 80 x 10^{-11} cc.cm/cm^3.sec.mm Hg, the index of refraction is 1.35 ~ 1.52, and the Vickers hardness No. is 4 ~ 25.

The raw material monomer (I) in the present invention is produced as follows.

That is, a fluorine-containing methacrylic acid ester is produced as in the following example. Tetrafluoroethyleneoxide and hexafluoropropyleneoxide generate perfluoropolyether (1) in the presence of FCO (CF_2)n COF and fluorine anion. This is used as the iodide (2); it is allowed to react with allyl acetate, and introduced, as it is well-known, into the compound (3) having an epoxide group (for example, J. Org. Chem., 27, 3033 (1962)).



(In the above formula, A, B, and X are identical with the above.)

Furthermore, the resultant fluorine methacrylic acid ester (I) can be obtained by treating diepoxide (3) with a slight excess amount of methacrylic acid reactive derivatives, for example, methacrylic acid halide (e. g., methacrylic acid chloride) or ethylene glycol monomethacrylate and alkali (e. g., sodium hydrate, potassium hydrate, triethylamine, etc.).

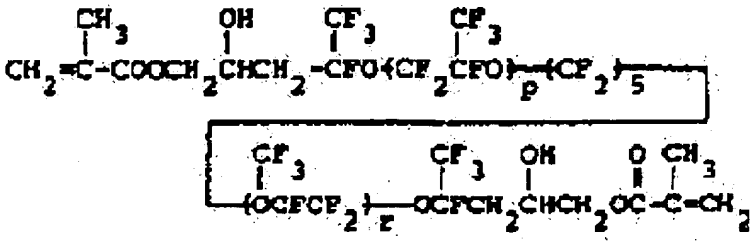
The polymer of the present invention consisting of monomer (I) has excellent oxygen permeability, hydrophilic property, and wetness property. It is also makes the molding and mechanical processing simple.

The polymer is useful as an oxygen-permeable substance for medical use (for example, an oxygen-permeable substance in the ophthalmic field, such as HLC).

The production of the oxygen-permeable substance for medical use made of such a polymer, particularly for the production of HLC, can be carried out with a well-known process and molding.

Application Example 1

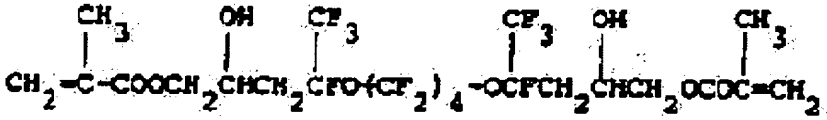
After thoroughly mixing 1.5 g of monomer (3) (p + r = 8), namely, the monomer represented by the following formula:



0.6 g of propyl-bis(trimethylsiloxy) methylsilane, 1.7 g of methyl methacrylate, 0.2 g of benzyl methacrylate, 0.2g of ethylene glycol dimethacrylate, and 20 mg of azobisisobutyronitrile, it is allowed to freeze in a dry ice – acetone bath, then deaerated by using a vacuum pump for five minutes at approximately 1 mm Hg. The experimental tube inside is allowed to return to normal temperature and is melted under vacuum. The freezing, deaeration, and melting process is repeated for four times until there is no occurrence of air bubbles. After being sealed under vacuum, it is heated at 50 ^{0}C for 24 hours, then at 70 ^{0}C for 5 hours, and at 90 ^{0}C for 8 hours. The produced polymer is allowed to dry at a reduced pressure of approximately 1 mm Hg, at 100^{0}C for 24 hours. A slightly yellowish transparent material is obtained. The Vickers hardness No. is 13, and the oxygen permeability coefficient is 16 x 10^{-10} cc.cm/cm^3.sec.mm Hg. This material was used for producing HCL.

Application Example 2

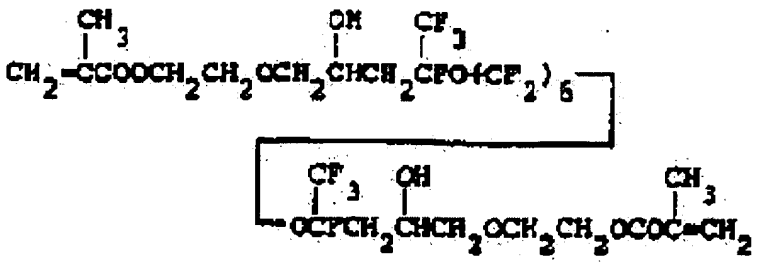
After thoroughly mixing 1.6 g of monomer (1), namely, the monomer represented by the following formula:



0.2 g of N–vinylpyrrolidone, 0.9g of 3–(methacryloxy) propyl bis(trimethylsiloxy) methylsilane, 1.4 g of methyl methacrylic acid, 0.2g of allyl methacrylate, and 27 mg of azobisdimethylvaleronitrile, the same treatment as in Application Example 1 is conducted. A colorless transparent material is obtained. The oxygen permeability coefficient is 11 x 10^{-11} cc.cm/cm^3.sec.mm Hg, and the Vickers hardness No. is 13.0. This material was used for producing HCL.

Application Example 3

After thoroughly mixing 1.1g of monomer (2), namely, the monomer represented by the following formula:



2.0g 2–hydroxyethyl methacrylate, 0.7g of 3 – (methacryloxy) propylbis (trimethylsiloxy) methylsilane, 0.2g of ethylene glycol dimethacrylate, and 20 mg of azobisbutyronitrile, the same treatment as in Application Example 1 is conducted. A slightly yellowish transparent material is obtained. The oxygen permeability coefficient is 18.3×10^{-11} cc.cm/cm^3.sec.mm Hg, and the Vickers hardness No. is 11.3. This material was used for producing HCL.